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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BASI, NIRMAL SINGH	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,847	TORAN-ALLERAND, C. DOMINIQUE	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 9/7/07.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 10-13 and 42 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 10-13 and 42 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed 9/07 has been entered. Applicant has amended claims10 and 12, added new claim 42 and cancelled claims 1-9 ands 14-41. Claims 10-13 and 42 are pending.

Claim Rejection, 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 10-13 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 12 are indefinite for use of the term "molecular weight of 62-63kDA". The term "molecular weight of 62-63kDA" does not provide sufficient structural and functional information about the protein so as to allow the metes bounds of the claim to be determined. The molecular weight of a protein depends upon the method used for said determination. For example, the molecular weight of a protein may differ if determined by polyacrylamide gel electrophoresis under denaturing condition as compared to under non-denaturing conditions. Centrifugation techniques such as sedimentation velocity or sedimentation equilibrium may again give a different molecular weight. The molecular weight calculated directly based on the amino acids present in a protein may again be different. The method used for determining molecular weight has not been disclosed.

Claims 10 and 12 are indefinite because it is not clear if the "designated 6F11"

refers to the "monoclonal antibody" or to the "estrogen receptor alpha" so as to allow the metes bounds of the claim to be determined.

Claims 10 and 12 are indefinite because it is not clear what signal indicates that the agent is an agonist or antagonist of the plasma membrane receptor ER-X. It is not clear what "detectable signal" is generated upon formation of the complex between the receptor and the known ligand.

Claim 10 is indefinite because it is not clear if the "contacting the plasma membrane receptor ER-X with agent " occurs in the presence of a known agonist or if the conditions that would allow the formation of a complex between the plasma membrane receptor ER-X with a known agonist were first determined and said conditions, in the absence of agonist, used when contacting the plasma membrane receptor ER-X with the agent.

Claims 11, 13 and 42 are rejected for depending on an indefinite base claim.

Claim Rejection, 35 U.S.C. 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-13 and 42 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether an agent is an agonist or antagonist of the one species of the plasma membrane associated estrogen receptor (ER-X) disclosed in the specification as having a molecular of 62-63kDa determined by SDS-PAGE, wherein the ER-X is isolated by contacting a neocortex

tissue lysate from an estrogen receptor-α knockout mouse with a murine monoclonal antibody (designated 6F11 and raised against estrogen receptor alpha (ER-α)) under conditions which permit the formation of a complex between the 6F11 antibody and ER-X; (ii) capturing the complex between the 6F11 antibody and ER-X with an anti-mouse IgG-coated polystyrene magnetizable bead; (iii) precipitating the complex; and (iv) separating ER-X from the complex based upon molecular size, does not reasonably provide enablement for the use of ER-X receptors defined by other means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 10-13 and 42 recite a method for determing whether an agent is an agonist or antagonist of cell-surface estrogen receptor ER-X defined by a molecular weight of 62-63kDa and is obtainable by (i) contacting a neocortex tissue lysate from an estrogen receptor-α knockout mouse with a murine monoclonal antibody raised against estrogen receptor alpha (ER-α) designated 6F11 under conditions which permit the formation of a complex between the 6FII antibody and ER-X; (ii) capturing the complex between the 6FII antibody and ER-X with an anti-mouse IgG-coated polystyrene maqnetizable bead; (iii) precipitating the complex; and (iv) separating ER-X from the complex based upon molecular size.

The term "molecular weight of 62-63kDA" does not provide sufficient structural and functional information so as to define the ER-X. The molecular weight of a protein depends upon the method used for determination of said weight. For example, the

molecular weight of protein may differ if determined by polyacrylamide gel electrophoresis under denaturing condition as compared to under non-denaturing conditions. Centrifugation techniques such as sedimentation velocity or sedimentation equilibrium may again give a different molecular weight. The molecular weight calculated directly based on the amino acids present in a protein may again be different. The method used for determining molecular weight has not been disclosed in the claim.

Further, the limitation of "obtainable" when defining the receptor by functional limitations leaves open the possibility that it has been obtained by other means. The specification discloses, "The theoretical existence of membrane ERs has been suggested in the literature for the past twenty-five years (Anuradha, 1994; Pietras, 1977; and Watson, 1999). However, to date, no conclusive evidence has demonstrated whether these theoretical membrane ERs exist as a small subpopulation of both ER-α (Watson, 199-9) or ER-β, or in fact represent novel members of the ER family (Das, 1997; and Gu, 1999). Singh et al. and Toran-Allerand have suggested that. an estrogen receptor subtype, designated "ER-X", would be expected to exist in neocortical cells, but have provided no characterization of this suggested entity (Singh, 1999; Singh, 2000; and Toran-Allerand, 2000)." Applicants have identified a new receptor, ER-X, by a complex set protocol disclosed on pages 32-37. Applicants have one ER-X receptor with specific functional characteristics obtained by a set protocol, but the claims as written encompass many species of the receptor because of the description, only by molecular weight, of the ER-X. Although the claims recite "obtainable" when referring to a method of isolation of the ER-X receptor, this does not limit the ER-X to the one

isolated by applicant. As argued above, even the molecular weight has ambiguity. The instant fact pattern is similar to that in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure or technique (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a). The specification discloses that a specific ER-X needs to be present in order to determine agonistic or and antagonistic activity. The specification also discloses specific conditions are required to isolate the ER-X. However, the claims fail to recite all the limitations that either define the ER-X so that the skilled artisan can know its structure or sufficient limitations to purify the ER-X, and thus the skilled artisan would have to resort to trial to identify or purify the polypeptides encompassed by the claimed method. At the time of the invention, the state of the art established that ER-X was novel with no known defined structure or means for isolation and purification. While it is known in the art that proteins can be purified using various conditions and purification schemes, they requires specific conditions and specific purification schemes to achieve high yields, purity and functional protein.

Due to the large quantity of experimentation necessary to isolate other members of the ER-X family because of the lack of direction/guidance presented in the

specification regarding specific conditions other than those recited in claims 10-12, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of specific conditions on protein purification, and the breadth of the claims which fail to specifically define s ER-X, undue experimentation would be required of the skilled artisan to make and/or use other species of ER-X in the claimed invention in its full scope.

The deposit of biological 6F11antibody (Novacastra, Vector Laboratories, Burlingham, Ca) is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the 6F11antibody. The deposit of 6F11antibody is not in full compliance with 37 CFR 1.803-1.809 because the specification does not provide a repeatable method for obtaining 6F11antibody in the future. Although, the aforementioned antibody, if available today from Novacastra, Vector Laboratories, Burlingham, Ca, may not be available in the future. An enabled deposit would satisfy the requirements of 35 USC 112, first paragraph.

To overcome the rejection Applicant must provide evidence that 6F11antibody listed in instant application will be available under the criteria (I)-(V) listed below. Although, the aforementioned 6F11antibody if available today from Novacastra, Vector Laboratories, Burlingham, Ca, may not be available in the future. An enabled deposit would satisfy the requirements of 35 USC 112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent,

would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(I) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(II) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(III) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(IV) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(V) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

4. No claim is allowed.

Advisory

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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CHRISTINE J. SAOUD
PRIMARY EXAMINER